

Assessment and Treatment of Alcohol and Drug Withdrawal

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Treatment usually consists of the following components:

- **Assessment** – Assessment and diagnosis
- **Intervention** - Initiation of treatment and/or referral
- **Detoxification** - Removal of alcohol or drug from the body and the treatment of withdrawal
- **Rehabilitation** - Medical, psychological and social measures to help avoid the use of psychoactive substances in the future

Medications are being increasingly used to assist detoxification and rehabilitation.

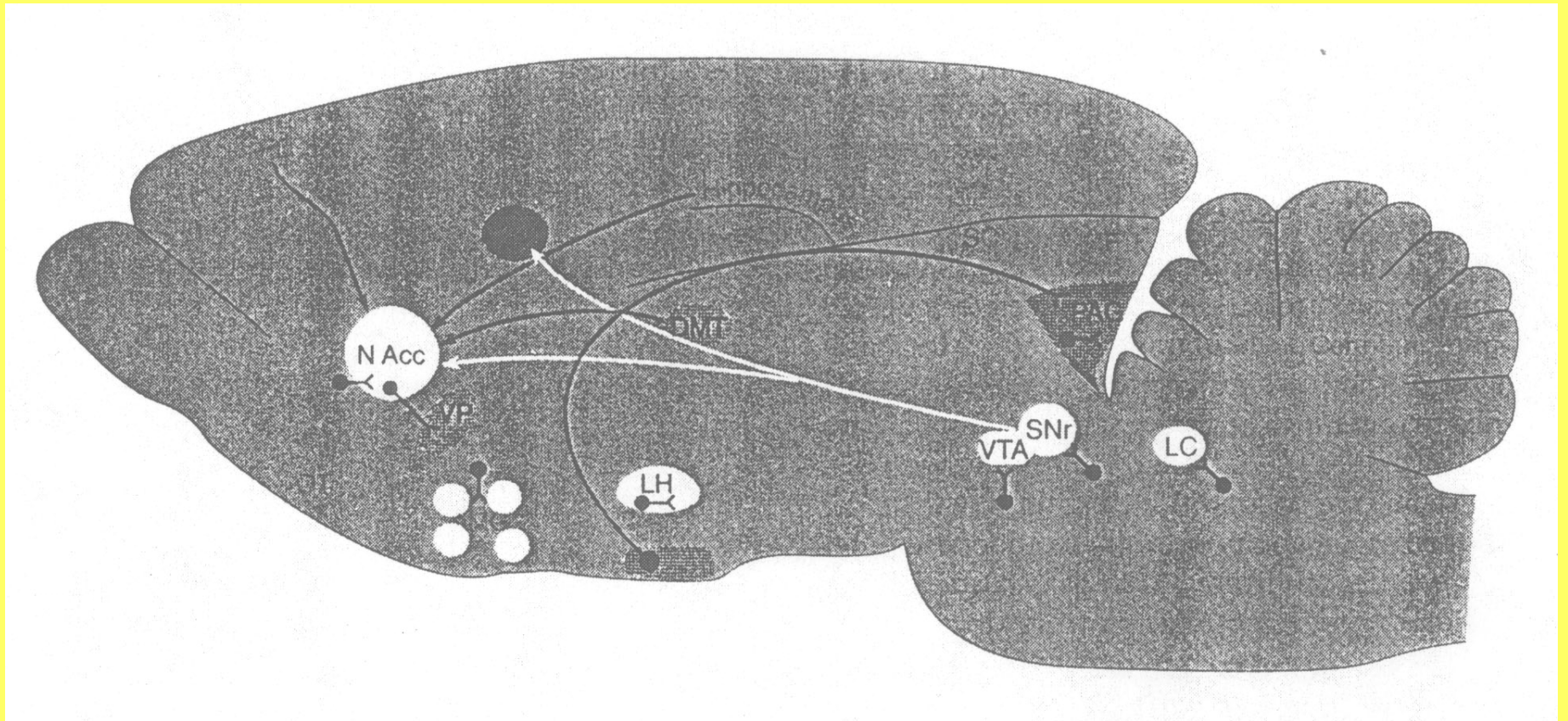
Withdrawal

- A distinct physiological and/or behavioral state that follows cessation or reduction in the amount of drug used.
- In general, the effects of withdrawal are the opposite of those that the drug produces (i.e. withdrawal from depressants produces excitation).
- Chronic use of many non-abused pharmacological agents including beta-blockers, anti-histamines, anti-arrhythmics, and antidepressants may be associated with a withdrawal syndrome following drug discontinuation.

Neurotransmitters and Receptors Affected By Drugs and Alcohol

- Acetylcholine
- Adenosine
- Dopamine
- Gamma-aminobutyric acid (GABA)
- Glutamate
- Norepinephrine
- Opioid peptides
- Serotonin (5HT)

Brain Structures Associated with Drug and Alcohol Dependence



Detoxification Treatment

- Primary goal is to achieve a drug-free state to manage acute withdrawal signs and symptoms and to prepare patients for further treatment
 - wide spectrum of severity
 - drug-specific syndromes: opiates, cocaine, alcohol, benzodiazepines
- Pharmacological agents are commonly used for the treatment of withdrawal

Methods of Detoxification - I

- **Controlled administration of the drug, with slow taper in daily drug dose.**

(Examples: gradually cutting back on alcohol, tapering sedatives in sedative dependence, nicotine fading)

2. Administration of a cross-tolerant, agent that is slowly tapered over time.

(Examples: chlordiazepoxide (Librium®) for alcohol withdrawal, methadone in opioid withdrawal)

Methods of Detoxification - II

3. Administration of an alternate agent to suppress withdrawal signs and symptoms

(Examples: clonidine in opioid withdrawal, anticonvulsants in alcohol and sedative withdrawal).

4. Non-medicated detoxification, with supportive care

(Examples: social setting detoxification in alcohol dependence; non-medicated alcohol detoxification is common in England).

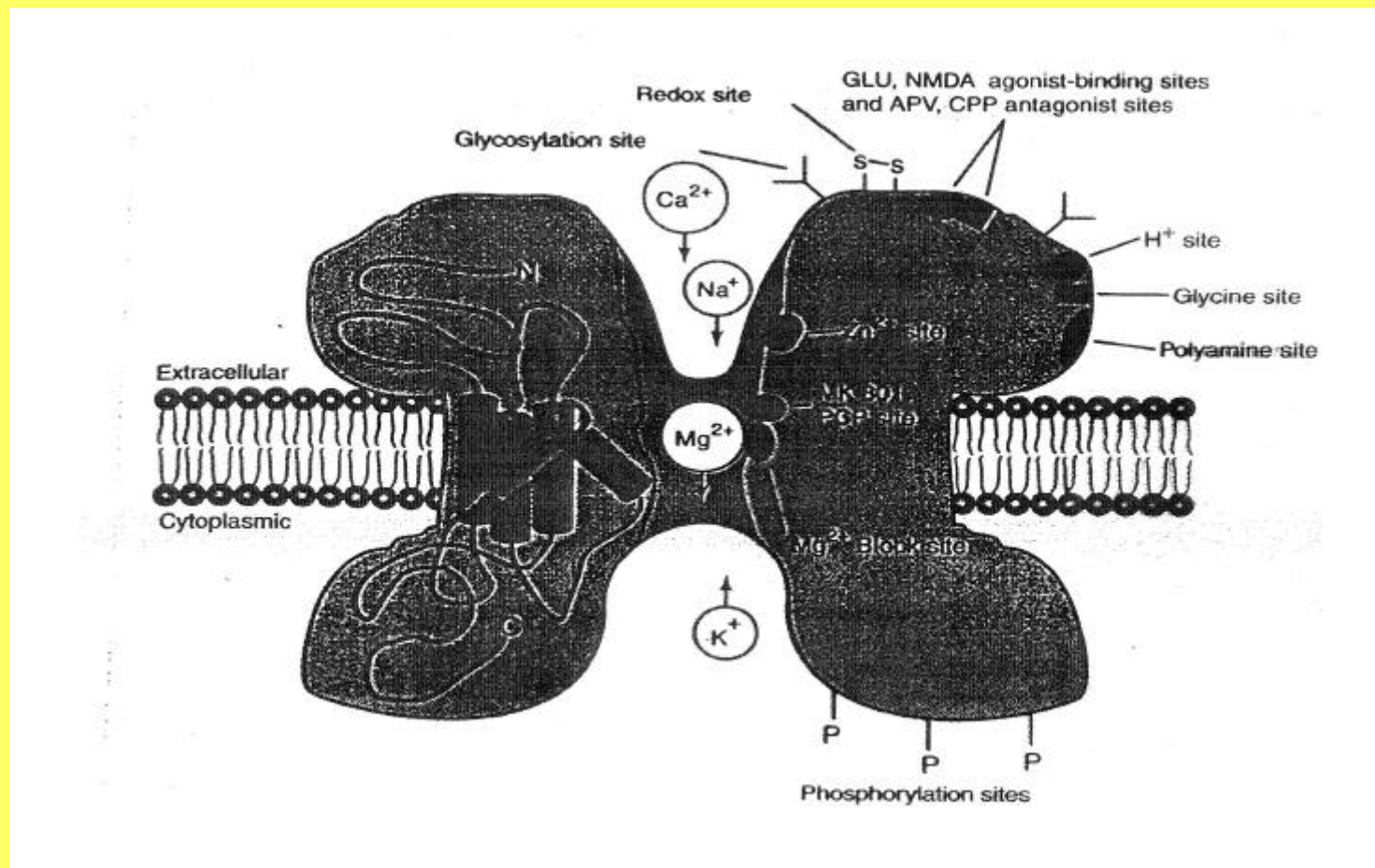
Alcohol Withdrawal Syndrome I

- A syndrome of specific signs and symptoms that follows the cessation of, or reduction of dose in regularly consumed alcohol
- Includes adrenergic hyperactivity:
tachycardia, hypertension, tremor, sweating
- Includes mental status changes:
anxiety, restlessness, confusion, hallucinations, disorientation
- Can be fatal in severe cases, but fatalities are rare

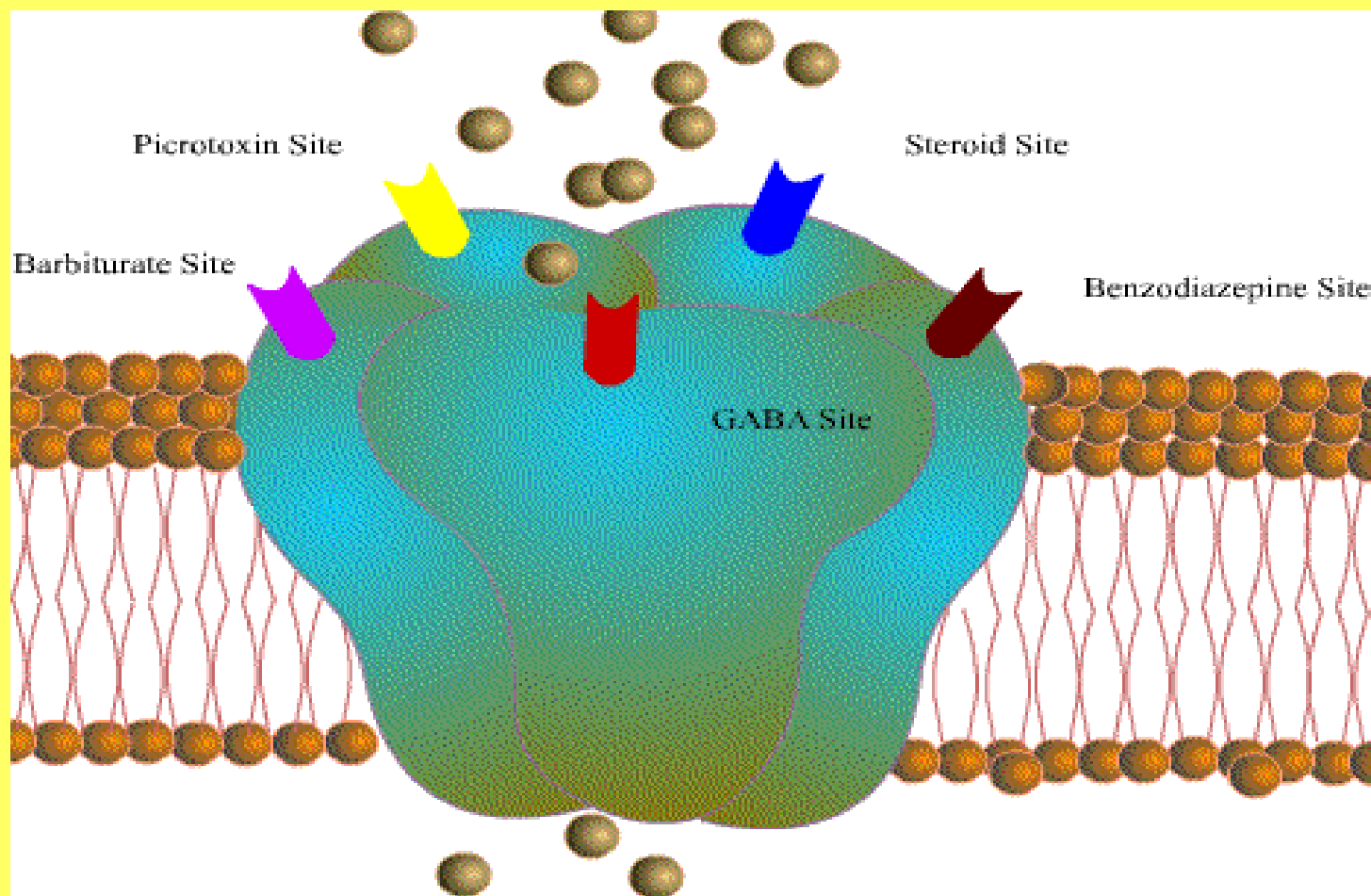
Alcohol Withdrawal Syndrome II

- Withdrawal shows a wide spectrum of severity
- Withdrawal is due to chronic adaptive changes in neurotransmitter receptors (especially GABA and glutamate) after chronic alcohol consumption
- Worsens with repeated episodes (kindling hypothesis)

The NMDA- Glutamate Receptor is inhibited by acute alcohol and up- regulated (supersensitive) during alcohol withdrawal



GABA Receptor activity is facilitated by acute alcohol and down-regulated (subsensitive) during alcohol withdrawal



Alcohol Detoxification

Initial Assessment

- History
 - Type and amount of substances used, level of dependence, CIWA score
 - Number of previous detoxifications, presence of seizures or DTs
 - Social history, domicile(shelter OK), social supports
 - Presence of psychiatric disorders, depression, anxiety, psychosis, suicidality
 - Ability to follow instructions, ability to come to clinic daily
- Physical Examination
 - Vital signs - afebrile, normotensive: SBP<180, DBP<110
 - Presence and severity of hepatic disease (cirrhosis, hepatitis) GI bleeding
 - Presence of other disease, cardiac, pulmonary, infections etc.
 - Able to tolerate oral medication
- Laboratory Examination
 - CBC, diff, platelet count ok
 - LFTs < 3x normal; bilirubin < 3.0
 - Electrolytes OK, creatinine < 2.0
 - Alcohol level (blood or breath), urine tox screen

Medications Commonly Used for Alcohol Withdrawal Treatment-I

- No medication
- Long-acting Benzodiazepines
 - chlordiazepoxide (Librium®)
 - diazepam (Valium®)
- Short Acting Benzodiazepines
 - lorazepam (Ativan®)
 - oxazepam (Serax®)
- Barbiturates
 - phenobarbital
- β -adrenergic blockers
 - atenolol (Tenormin®)
 - propranolol (Inderal®)

Medications Commonly Used for Alcohol Withdrawal Treatment-II

- **α -2-adrenergic agonists**
 - clonidine (Catapres®)
- **Antiepileptic Drugs**
 - carbamazepine (Tegretol®)
 - valproic acid (Depakote®)
- **Vitamins**
 - Thiamine, pyridoxine (B6), B12, folate
- **Minerals**
 - Magnesium (Mg⁺⁺)
 - Zinc (Zn⁺⁺)

Medications Commonly Used for Alcohol Withdrawal Treatment-III

- Neuroleptics for hallucinosis
 - haloperidol (Haldol®)
 - droperidol (Inopsine®)
- Antiemetics
 - phenergan
 - compazine
- Hypnotics for sleep
 - trazodone (Desyrl®)
 - Antihistamines (Benadryl®, Vistaril®)
 - benzodiazepines

Use of Withdrawal Scales

Clinical Institute Withdrawal Assessment (CIWA)

- Developed to quantify withdrawal intensity to guide need for medication
- Measures 10 withdrawal associated items: nausea/vomiting; tremor; sweating; anxiety; agitation; headache; tactile disturbances; auditory disturbances; visual disturbances; and clouding of sensorium
- Useful to quantify effects of medications
- Provides supportive care

(Sullivan, Brit J Addiction 84:1353-1357, 1989)

Treatment of (Uncomplicated) Alcohol Withdrawal Syndrome

- Fluids & nutrition (thiamine 100 mg qd x 3d; MVI)
- Reduce stimulation: quiet, dim light, few interruptions
- Reorientation, reassurance
- Comfort, analgesics
- Monitor symptoms with ratings (CIWA-Ar)
- Benzodiazepines for CIWA score >8

Treatment of Alcohol Withdrawal Delirium

- Good evidence for efficacy of benzodiazepines e.g., diazepam 10-20 mg PO or IV; lorazepam 1-2 mg Q1-2 hr PO, IV, or IM
- Good evidence for efficacy of haloperidol 1-2 mg Q1-2 hr PO, IV, or IM
- Key is to aggressively evaluate and treat other causes of delirium such as pneumonia, UTI, subdural hematoma, hepatic failure, Wernicke's encephalopathy

Anton and Becker, 1995

Treatment of Alcohol Withdrawal Seizures

- Good evidence for efficacy of benzodiazepines in prevention of seizures if no prior history of seizures
- No evidence of benefit of MgSO_4 [2 mg IM q 6h] to prevent seizures in patients without hypomagnesemia
- If prior history of adult seizure (due to AWS or not), addition of DPH 100 mg TID superior to chlordiazepoxide
- Continued anticonvulsant therapy after withdrawal seizures is not necessary without seizure disorder

Sedative Withdrawal Syndrome (SWS)

Clinical Symptoms

Uncomplicated SWS

- Gross tremor
(hands, tongue, eyelids)
- Hypertension
- Tachycardia
- Anxiety
- Sleep disturbance
- Irritability
- Hyperreflexia
- Sweating
- Nausea / vomiting

Complicated SWS

- Hallucinations
- Seizures
- Delirium

Sedatives: Use Freq. & Withdrawal Course

Drug	Usual freq. of use (hr)	Appearance of WD sx's (hrs)	Peak (hrs)
lorazepam	2-6	2-6	8-12
diazepam	4-8	8-12	8-12
alprazolam	6-8	8-20	8-12
pentobarbital	1-6	1-6	3-12
phenobarbital	6-12	6-12	24-48

Treatment of Sedative Withdrawal Syndrome

Medications

1. Benzodiazepines--necessary in moderate SWS
 - All benzos equipotent at adequate doses
 - Diazepam 10 mg PO or IV, q 1-2 hr or
 - Lorazepam 2 mg PO, or IV, Oxazepam 15-30 mg p.o.
q 1-2 hr if cirrhotic or elderly, to minimize accumulation of active desmethylated metabolites of long-acting benzos in these patients.
2. Pentobarbital-phenobarbital detoxification: for severe sedative dependence only--must be done as inpatient.

Treatment of Severely Dependent Sedative Addicts: Barbiturate Tapering

Assess dependence Severity

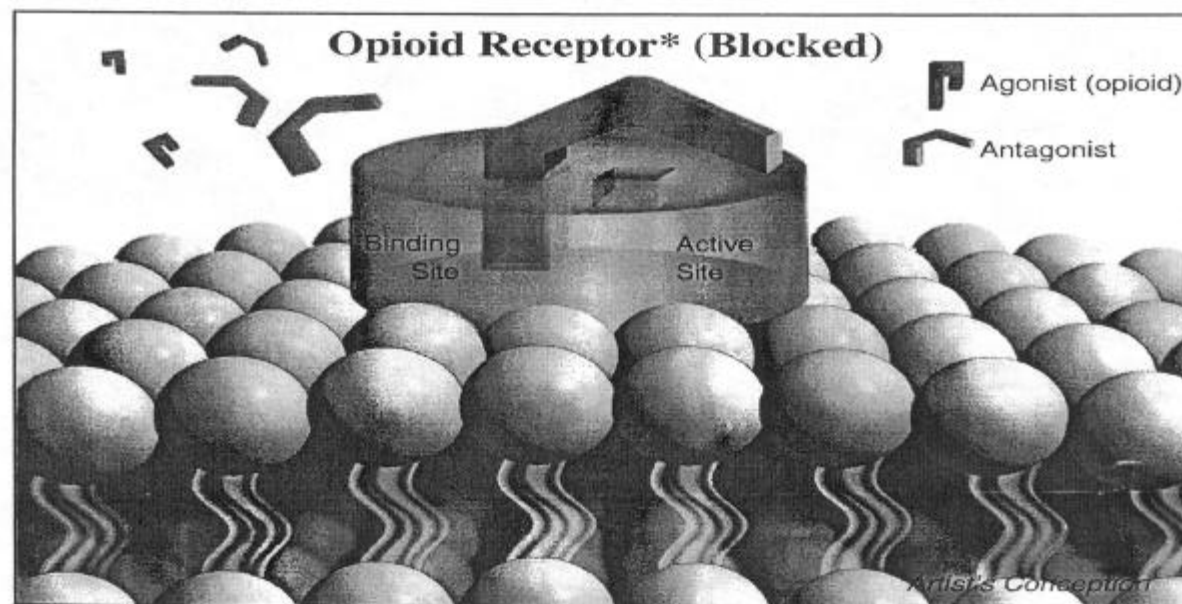
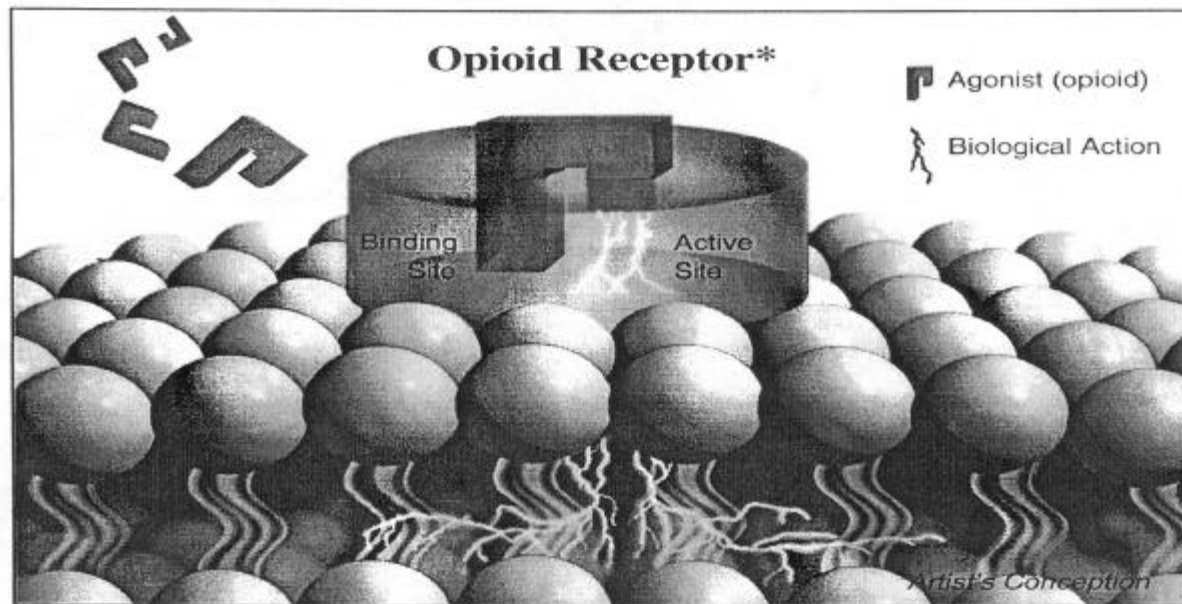
- oral dose of 200 mg pentobarbital, with evaluation 1 h after dose: if sleepy or nystagmus, tolerance is mild; If no nystagmus, give 2nd dose and assess after 1 hr. If sleepy or nystagmus, tolerance is moderate. If no nystagmus, give 3d dose and assess after 1 hr. If sleepy or nystagmus, tolerance is severe. If no nystagmus, tolerance very severe.

Initial Detoxification with Pentobarbital TID x 3d

- Dose is 200 mg for mild, 400 for moderate, 600 for severe, and 800 for very severe cases

Final Detoxification with Phenobarbital PO TID

- On day 4 and 5, give phenobarbital in doses $\frac{1}{3}$ of the total dose of pentobarbital employed
- Then taper 20%/day x 5d, monitoring tremors and nystagmus



Opioid Receptors and Ligands

Receptor subtypes	Agonists	Antagonists	Second messengers
mu-opioid	DAGOL Beta-Endorphin	Naloxone, Naltrexone	(-ve)cAMP, (+ve)gK ⁺
delta-opioid	DPDPE enkephalins	Naltrindol	(-ve)cAMP, (+ve)gK ⁺
kappa-opioid	U69593, dynorphinA 1-32	Norbinaltorphimine	(-ve)gCa ²⁺

Opiate Withdrawal Syndrome

Objective Signs

(observable and not easily feigned)

Increased BP

Increased Pulse

Increased Temperature

Piloerection ("gooseflesh")

Increased Pupil Size

Rhinorrhea

Lacrimation

Tremor

Insomnia

Diarrhea

Vomiting (Sometimes self-induced)

Seizures (meperidine or propoxyphene only--
or consider EtOH/sedatives)

Subjective Symptoms

(not observable or may be
feigned)

Nausea

Muscle ("bone") aches

Abdominal (stomach) cramps

Irritability

Anorexia

Weakness/Fatigue

Restlessness

Headache

Dizziness/Lightheadedness

Sneezing

Hot or Cold Flashes

Opiate Craving

Opiates: Use Freq. & Withdrawal Course

Drug	Usual freq. of use (hr)	Appearance of wdwl sx's (hrs)	Peak (hrs)
meperidine	2-3	4-6	8-12
hydromorphone	3	4-5	
heroin	4	8-12	48-72
morphine	5-6	14-20	
codeine	3	24	
methadone	8-24	36-72	72-96

Opiate Withdrawal Equivalencies

1 mg methadone is equivalent to:

heroin 1-2 mg

morphine 3-4 mg

hydromorphone 0.5 mg

codeine 30 mg

meperidine 20 mg

paregoric 7-8 cc

oxycodone 5 mg

laudanum 3 cc

dromoran 1 mg

levodromoran 0.5 mg

Pantopon 4 mg

Leritine 8 mg

From: Kleber, 1994

Evaluation of the Opiate Addict

History

Recent drug use: type(s) of drug(s) used
dose(s) and frequency

length of time used

date/time of last use, route, purpose, adverse effects

previous treatment/detoxifications

Other Medical & Psychiatric History (esp. depression)

Non-judgmental, sensitive approach

Social history: living arrangements, work status,
sexual orientation, friends (supportive?), family, legal

Evaluation of the Opiate Addict

(continued)

Complete physical exam:

Skin: needle tracks & marks, tattoos, hand edema, burns, piloerection, jaundice, abscesses

HEENT: cheilosis, thrush, nasal septal irritation or ulceration

CV: heart murmur (endocarditis), thrombophlebitis

Pulmonary: TB, pneumonia, edema

GI: hepatitis, cirrhosis, pancreatitis, diarrhea

Neuro: CNS infections, seizures, neuropathies

Lymphatic: adenopathy

Drug Treatment for Opiate Withdrawal

- Opioids – Opioid taper, substitution
- Clonidine
 - 0.1 mg. test dose
 - then 0.2 mg. three times a day x 3-5 days, and
 - #2 clonidine patch for 14 days
- Promethazine
 - 25 mg. IM for nausea
- Benzodiadepines
 - PO or IV for anxiety, restlessness
- Ibuprofen
 - 800 mg. for muscle cramps and joint pain

Methadone Detoxification

- Legal only on inpatient basis or in methadone program
- Must be completed within 21 days if inpatient
- Not indicated during pregnancy--maintenance preferred
- For street opiate addict: initial dose 10-40 mg po qd-bid as liquid

[If unsure of physical dependence, challenge with 0.2-0.4 mg naloxone SQ and observe for 1 hour]

- Effectiveness increases with length of taper

Clonidine Detoxification

- Can be performed as inpatient or outpatient
- Contraindicated if history hypotension, heart disease
- Initial dose is 0.1-0.2 mg po q 3 hr up to 1 mg on day 1 or peak of 10-15 mcg/kg/d in 3-6 divided doses
- Effect noted in 30 min and peak in 2-3 hr
- Beware low BP, esp. w/ 1st dose: observe 1-2 hrs
- Can use transdermal (TTS) patches (12 hour onset)
- After day 4, reduce dose by 25-30% QD, reducing HS dose last - can supplement with benzodiazepines, hypnotics, NSAIDs, antiemetics, ant motility agents
- Is also useful in facilitating early naltrexone induction

Buprenorphine

- Partial mu agonist, partial kappa antagonist
- High receptor affinity - displaces morphine and methadone from receptors
- Parenteral preparation useful in opioid detoxification and prevention of withdrawal
- Withdrawal syndrome is mild
- Has ceiling effects on agonist properties
- Oral preparation in trials for long-term maintenance treatment in opiate addicts

Buprenorphine Detoxification

- Beginning dose: 0.125 mg sc/im q3-4 hours, increasing as necessary to suppress WD
- New sublingual preparation: 2-6 mg/d SL x 2-3 days.
- Then taper over 3-4 days
- Naltrexone 12.5-50 mg QD in escalating doses - may be initiated on day 3 or 4 of taper

Ultra-Rapid Opioid Detoxification (UROD) Components

- Opioid antagonists (naloxone, naltrexone, nalmeffene) to rapidly reset opioid receptors
- General inhalation anesthesia to block withdrawal signs and symptoms
- Benzodiazepines for sedation and anxiolysis
- Clonidine to block adrenergic discharge
- No randomized efficacy studies, outcome
- Several deaths reported